

AMENDMENTS TO THE CLAIMS

1. (Previously presented) An *in vitro* method for generating a mutation in a gene of interest in a hypermutable cell and subsequently stabilizing the genome of the cell comprising the steps of:

growing a hypermutable mammalian cell comprising the gene of interest and a dominant-negative allele of a *PMS2* mismatch repair gene under control of an inducible transcriptional regulatory element;

testing the cell to determine whether the gene of interest harbors a mutation; and
restoring mismatch repair activity to the cell by decreasing expression of the dominant-negative allele, thereby generating a mutation in the gene of interest and stabilizing the genome of the cell.

2. (Original) The method of claim 1 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

3. (Original) The method of claim 1 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

4. (Original) The method of claim 1 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

5. (Original) The method of claim 1 wherein the step of testing comprises analyzing the phenotype of the cell.

6. (Currently amended) The method of claim 1 wherein the mammalian cell is made hypermutable by the process of introducing a polynucleotide comprising ~~a~~ said dominant-negative allele of a *PMS2* mismatch repair gene under control of an inducible transcriptional regulatory element into a mammalian cell *in vitro*, whereby the cell becomes hypermutable.

7. (Previously presented) The method of claim 6 further comprising the step of

introducing a reporter gene interrupted with a polymononucleotide tract which causes a reading frame-shift into the mammalian cell to permit the monitoring of hypermutability.

8-50. (Cancelled)